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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SAJJADI, FEREYDOUN GHOTB	

ART UNIT	PAPER NUMBER
1633	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,250	NEMEROW ET AL.	
	Examiner	Art Unit	
	FEREYDOUN G. SAJJADI	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7,10-54,57-68 and 72-82* is/are pending in the application.

4a) Of the above claim(s) *1-7,10-54,57,59-68 and 72-79* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58 and 80-82* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Request for Continued Examination

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission and amendment filed on October 13, 2008, that includes a response to the office action dated June 11, 2008, have been entered. Claims 1-7, 10-54 and 57-68 and 72-82 are pending in the application. Claims 69-71 have been cancelled and claims 58 and 81 amended. No claims were newly added. Claims 1-7, 10-54, 57, 59-68 and 72-79 stand withdrawn from further consideration with traverse. Accordingly, claims 58 and 80-82 are under current examination. Applicants should note that the instant claims have been examined commensurate with the scope of the elected invention and the species of the invention, i.e. the last repeat of Ad37 (serotype D) and its modified form presented as SEQ ID NO: 48.

Response & Withdrawn Claim Rejections - 35 USC § 102

Claims 58 and 69 were rejected under 35 U.S.C. 102(e) as being anticipated by Vigne et al. (U.S. Patent No.: 6,911,199; effective filing date: Aug. 27, 1998), in the previous office action dated June 11, 2008. Applicants' cancellation of claim 69 renders its rejection moot. Applicants have amended base claim 58 to incorporate the new limitations of an adenovirus particle comprising a modification in the AB loop or the CD loop of the fiber knob, wherein the fiber knob modification is selected from the group consisting of K01 and K012, not taught by the reference of Vigne et al.; thus obviating the ground of rejection. Therefore, the previous rejection is hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejection.

Response & Withdrawn Claim Rejections - 35 USC § 103

Claims 58 and 69-70 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vigne et al. (U.S. Patent No.: 6,455,314; effective filing date: Aug. 27, 1998), in view of Wickham et al. (U.S. Patent No: 2002/0132343; effective filing date Sep. 11, 1998), in the previous office action dated June 11, 2008. Applicants' cancellation of claims 69-70 renders their rejection moot. Applicants have amended base claim 58 to incorporate the new limitations of an adenovirus particle comprising a fiber knob modification selected from the group consisting of K01 and K012, not taught by the reference of Vigne et al. and Wickham et al.; thus obviating the ground of rejection. Therefore, the previous rejection is hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejection.

Claims 58 and 80-82 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vigne et al. (U.S. Patent No.: 6,455,314; effective filing date: Aug. 27, 1998), in view of Havenga et al. (U.S. Patent Publication No: 2003/0017138; filed Jul. 7, 1999), in the previous office action dated June 11, 2008. Applicants have amended base claim 58 to incorporate the new limitations of an adenovirus particle comprising a fiber knob modification selected from the group consisting of K01 and K012, not taught by the reference of Vigne et al. and Havenga et al.; thus obviating the ground of rejection. Therefore, the previous rejection is hereby withdrawn. Applicants' arguments are moot in view of the withdrawn rejection.

Response & Maintained Claim Rejections - 35 USC § 103

Claims 58 and 69-71 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Vigne et al. (U.S. Patent No.: 6,455,314; effective filing date: Aug. 27, 1998), in view of Hallenbeck et al. (U.S. Patent No: 2002/0137213; effective filing date June 2, 2000). Applicants' cancellation of claims 69-70 renders their rejection moot. The rejection set forth on page 6 of the previous office action dated June 11, 2008 is maintained for claim 58 for reasons of record.

Applicants have introduced the limitations of cancelled claims 69-71 into base claim 58. Applicants traverse the rejection, arguing that the references alone or in combination do not teach all of the elements of claim 58, namely a modified adenovirus fiber in which modification is a mutation, insertion or replacement of at least one amino acid in a fiber shaft 13-repeat corresponding to the last full 13 repeat, and wherein the fiber further comprises a modification in the AB loop or the CD loop of the fiber knob, wherein the fiber knob modification is selected from the group consisting of K01 and K012, whereby binding of the modified fiber to CAR is reduced.

Applicants' arguments have been fully considered, but are not found persuasive.

Applicants have failed to specifically and distinctly identify which particular elements of base claim 58 are allegedly missing from the combined teaching of the references. Vigne et al. describe targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein that include short targeting peptides fused to the C-terminus of the fiber protein, or the fiber H1 loop (knob) target the modified adenoparticles to specific cell types (Title and Abstract). Additionally disclosing substitution or replacement of the Ad5 shaft with Ad3, comprising a modification in the last full repeat of the fiber shaft (column 33). Vigne el al. further describe replacement of a part of the fiber 1-11 loop (knob) with a ligand peptide or targeting sequence, that impair the native entry pathway and provide an additional, CAR-independent, pathway of infection." (columns 47 and 48; bridging). Hallenbeck et al. describe adenovirus particles mutated in their fiber proteins that no longer bind to their natural cellular receptor and can be retargeted to a specific cell type through the addition of a ligand to the virus capsid (Abstract). Hallenbeck et al. specifically describe adenoviral constructs containing the KOI fiber AB loop mutation (Fig. 9), displaying a diminished interaction with CAR (paragraph [0092]). Adenoviral vectors containing the KOI mutation in conjunction with a ligand targeting moiety are described in Example 3.

Thus, the rejection of claim 58 is maintained for reasons of record and the preceding commentary.

New Claim Rejections - 35 USC § 103

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 58 and 80-82 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Vigne et al. (U.S. Patent No.: 6,455,314; effective filing date: Aug. 27, 1998), in view of Hallenbeck et al. (U.S. Patent No: 2002/0137213; effective filing date June 2, 2000), as applied to claim 58 above, and further in view of Havenga et al. (U.S. Patent Publication No: 2003/0017138; filed Jul. 7, 1999).

The claims as amended encompass an adenovirus particle comprising a modified adenovirus fiber in which modification is a mutation, insertion or replacement of at least one amino acid in a fiber shaft β-repeat corresponding to the last full β-repeat, and wherein the fiber further comprises a modification in the AB loop or the CD loop of the fiber knob, wherein the fiber knob modification is selected from the group consisting of K01 and K012, whereby binding of the modified fiber to CAR is reduced, and wherein the modification comprises replacement of the last full β-repeat with a corresponding repeat sequence form an Ad37 serotype D adenovirus, as set forth in SEQ ID NO: 48.

Vigne et al. describe targeted adenovirus vectors for delivery of heterologous genes, wherein modifications of the internal sites of the adenovirus fiber protein that include short targeting peptides fused to the C-terminus of the fiber protein, or the fiber HI loop (knob) target the modified adenoparticles to specific cell types (Title and Abstract). Specifically disclosing that the fiber protein can be modified to have a fiber shaft that is shorter than a wild-type fiber shaft, in particular by an in-frame deletion or by replacing it with the shaft from another serotype (column 6). Additionally disclosing substitution or replacement of the Ad5 shaft with Ad3, comprising a modification in the last full repeat of the fiber shaft (column 33). Vigne el al. further describe replacement of a part of the fiber 1-11 loop (knob) with a ligand peptide or targeting sequence, that impair the native entry pathway and provide an additional, CAR-independent, pathway of infection." (columns 47 and 48; bridging). With respect to modification of the last full repeat, Vigne et al. teach the fiber shaft as comprising pseudorepeats of 15 amino acids, which are believed to form two alternating β–strands and β –bends; and that the overall length of the fiber shaft and the number of repeats varies between different adenoviral serotypes

(column 2, lines 22-30). Vigne et al. further teach that the fiber protein can be modified to have a fiber shaft that is shorter than a wild-type fiber shaft, in particular by an in-frame deletion or by replacing it with the shaft from another serotype (column 6). Additionally teaching using SOE35Kg primer corresponding to the last repeat of the Ad3 fiber shaft and primers that include modifications resulting in the creation of restriction sites to generate an intertypic fiber composed of the Ad5 tail, the Ad3 shaft and part of the Ad5 knob, and flanked with unique restriction sites (columns 31 and 32, bridging). The disclosed mutation thus encompasses a substitution or replacement of the Ad5 shaft with Ad3, comprising a modification in the last full repeat of the fiber shaft.

Hallenbeck et al. describe adenovirus particles mutated in their fiber proteins that no longer bind to their natural cellular receptor and can be retargeted to a specific cell type through the addition of a ligand to the virus capsid (Abstract). Hallenbeck et al. specifically describe adenoviral constructs containing the KOI fiber AB loop mutation (Fig. 9), displaying a diminished interaction with CAR (paragraph [0092]). Adenoviral vectors containing the KOI mutation in conjunction with a ligand targeting moiety are described in Example 3.

While Vigne et al. and Hallenbeck et al. do not specifically describe the serotype D Ad37 virus having the sequence set forth SEQ ID NO: 48, such adenovirus serotype and sequences of the last full repeat of fiber shaft were known in the prior art.

Havenga et al. describe chimeric adenoviruses as vectors, wherein the hybrid adenoviruses contain a genome derived from different adenovirus serotypes, displaying a modified host range that overcome the limitations with currently used serotype C adenoviruses (Abstract). Havenga et al. state: "Preferably, the (chimeric) adenoviruses capable of transducing a CAR negative cell include at least an adenovirus receptor binding part of a fiber protein from an adenovirus of subgroup D" (paragraph [0020], further depicting the fiber shaft sequences of type 37 in Fig. 7, and specifically describing Sequence 31, comprising the last full repeat of instantly claimed SEQ ID NO: 48.

Therefore, it would have been *prima facie* obvious for a person of ordinary skill in the art, to combine the teachings of Vigne et al., Hallenbeck et al. and Havenga et al. to substitute or modify the last full repeat of the fiber shaft of a serotype 37 in a retargeted adenoviral vector, as

instantly claimed, with a reasonable expectation of success, at the time of the instant invention. A person of ordinary skill in the art would have been motivated to introduce a modification in the fiber shaft as taught by both Vigne et al. and Havenga et al., because such mutations would provide an additional CAR-independent pathway of infection for adenovirus retargeting.

Conclusion

Claims 58 and 80-82 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to FEREYDOUN G. SAJJADI whose telephone number is (571)272-3311. The examiner can normally be reached on 6:30 AM-3:30 PM EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Fereydoun G Sajjadi/
Examiner, Art Unit 1633